



Potential application of stereotactic radiotherapy in head and neck cancer

Marta Biedka-Paluch^{1,2} , Patryk Leszek Biedka²,
Beata Januszko-Giergielewicz³ 

1 Radiotherapy Department, Oncology Center – Prof. Franciszek Łukaszczyk Memorial Hospital, Bydgoszcz, Poland

2 Chair and Clinic of Oncology and Brachytherapy, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland

3 Academy of Applied Medical and Social Sciences, Elbląg, Poland

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Abstract

Introduction: Stereotactic ablative radiation (SABR) therapy, or stereotactic body radiation therapy (SBRT), delivers high-dose external beam radiation to a small, clearly defined target area in one or more sessions. It is the standard treatment for medically inoperable early-stage non-small cell lung cancer, early-stage prostate cancer, and oligometastatic disease from other primary locations.

Aim: This article discusses the use of stereotactic radiotherapy in neoplasms of the head and neck region – as primary treatment, including early laryngeal cancer; as post-operative adjuvant therapy; as a boost after radiation therapy (dose escalation method); and the use of SBRT for re-radiation therapy. The next part discusses the serious complication in the form of carotid artery rupture in the course of repeated radiotherapy.

Material and methods: The article was written based on the analysis of the literature on the subject from 2009 to 2021.

Results and discussion: SBRT is relatively safe and effective, especially in those cancers where the survival time with the cancer is relatively long, moreover, the location of the critical organs around the target of the therapy and the dose deposited in the critical organs is important.

Conclusions: (1) Treatment should be considered for patients receiving treatment more than 2 years after their primary treatment. (2) In cases with a shorter time interval, a minimum of 6 months should elapse before considering SBRT. (3) If feasible, tumor resection should be pursued. (4) In cases of non-resectable tumors, preservation of the functional organ should be a priority.

Corresponding author:

Marta Biedka-Paluch, Radiotherapy Department, Oncology Center – Prof. Franciszek Łukaszczyk Memorial Hospital, Romanowskiej 2, 85-796 Bydgoszcz, Poland.

Tel. +48 605 478 745.

E-mail: biedkam@co.bydgoszcz.pl

1. INTRODUCTION

Stereotactic ablative radiation therapy (SABR), also known as stereotactic body radiation therapy (SBRT), is a method of delivering high-dose external beam radiation. This therapy uses one or more fractions to a small, clearly visible area (target) and is the standard used in; early stage of medically inoperable non-small cell lung cancer (level 1); early stage prostate cancer (level 2); oligometastatic disease of other primary locations (level 2). Dr Lars Leksell developed the gamma knife therapy to treat intracranial lesion with ablative single-fraction radiation therapy back in 1950s, however SABR method was not used in other indications before 1990s, until investigators at the Karolinska Institute pioneered the use of single-fraction SBRT in extracranial tumors. Since then, there has been enormous development in the field of imaging and radiotherapy planning and high precision has allowed the use of SBRT in the treatment of extracranial tumors, which expands possibilities for the new localisations.^{1,2}

There is unsatisfactorily amount of information about the possibilities of SBRT in the head and neck cancer (HNC), which might be associated with its uncommon use. The reasoning behind lower usage of this method is: extent of the disease, mucosal spread and proximity of the disease to vital organs, it is important to emphasize that every method has its benefits and drawbacks (Table 1).

Neoplastic cells which are in different phases of cell cycle have different radiosensitivity, and the cells in the following days do not move to the next phases of the cycle, which are radio-sensitive as in the case of conventional radiotherapy. In good clinical practice, in order to reduce this negative effect, we tend to administer stereotactic radiotherapy in several fractions (3–7) than in one fraction.^{3–8}

2. AIM

The aim of this study is to display the clinical situation in which SBRT technique may be considered in the treatment of HNC cancers:

- (1) Primary radiotherapy;
- (2) Early laryngeal cancer;
- (3) Adjuvant treatment after surgery;
- (4) Boost treatment;
- (5) Repeat radiotherapy in recurrent cancers.

3. MATERIAL AND METHODS

The article was written based on the analysis of the literature on the subject from 2009 to 2021.

4. RESULTS AND DISCUSSION

4.1. PRIMARY RADIOTHERAPY WITH SBRT

Primary radiation therapy with SBRT has changed the way cancer is treated, including in early-stage lung cancer, while its use in cancers of the head and neck region is significantly limited. The role of SBRT as a primary treatment is evolving and there are individual reports of its use in case of patients who are medically inoperable for other forms of therapy and/or in the elderly people.^{2,9}

In these cases, we can take full advantage of the benefits such as: short treatment time, good clinical effect with little or no radiation exposure.²

Gogineni et al.¹⁰ presented a group of 66 patients with a median age of 80 years qualified for primary treatment with SBRT, who were administered 40 Gy in 5 fractions, two times per week, in addition, 48% received cetuximab or standard chemotherapy. The median follow-up time was 15 months (range 3–88 months), and local control (LC) was 68%, regional and distant control rates were 73% and 76%, respectively. The median time to local failure was 28.3 months. It is worth mentioning

Table 1. The advantages and disadvantages of stereotactic radiotherapy compared to conventional treatment.

The advantages of SBRT	The disadvantages of SBRT
<ol style="list-style-type: none"> 1. Shorter treatment time. 2. Achieve clinically meaningful tumor-specific immune responses. 3. Massive tumor cell death release of tumor antigens and inflammatory cytokines. 4. Increases tumor vascular permeability (increased extravasation of antigen-presenting cells and effector T cells). 5. Spare circulating lymphocytes due to smaller irradiated tissue volume and blood volume. 6. Lesser to none acute radiation reaction and/or side effects. 7. Reduction of laryngological examination and pharmacological treatment. 8. Lesser to none breaks in radiotherapy and / or its premature termination. 9. Shortening the treatment time reduces the probability of accelerated repopulation and better local control. 10. Radioresistant tumor, which relapse in previously irradiated area, needs higher fractional doses in re-radiation treatment. 	<ol style="list-style-type: none"> 1. Large number of hypoxic cells. 2. Neoplastic cells are in different phases of the cell cycle.

that one-third (32%) of relapses occurred in the irradiated area, and in case of 4 people – at the edge of the radiotherapy field. The treatment was well tolerated, no grade 4 or 5 toxicity was noticed and only 2 cases of patients (3%) developed grade G3 toxicity.¹⁰ The range of total doses and fraction doses used was similar to those in other publications and most often ranged from 19.5–50 Gy in 1 to 6 fractions. The results obtained in the studies are most often given by authors for one-year period and they are similar for both local control (1-year 46% to 87%) and overall survival (60%–85%).^{10–12}

An interesting analysis was performed by Siddiqui et al.,¹³ who assessed the role of: a single fraction at a dose of 13–18 Gy or a total dose of 36–48 Gy in 5–8 SBRT fractions in a heterogeneous patient population, including primary, recurrent or metastatic neoplasms of HNC. One-year tumor control observations were 83.3%, 60.6%, and 75.0% in the primary, relapsed, and metastatic groups, respectively. The median of overall survival was 28.7 months for primary tumors, 6.7 months for relapses, and 5.6 months for the metastatic groups. In this study, 10 patients received stereotactic radiotherapy as primary treatment with both single dose and multiple fractions (18–48 Gy in 1–8 SBRT fractions). One-year local control in the primary treatment LC group was 83%, and the one-year overall survival (OS) was 70%. In this group there was only one cataract grade 3 and one patient with pain in grade 3.¹³

The authors of the systematic review emphasize that there is no evidence of the use of stereotactic radiotherapy in primary HNC and therefore cannot be recommended as standard care, and the studies performed were small case series and studies in the phase 1.² Summarizing, the authors of the reports presented studies in a group of 3 to 66 patients and administered doses in the range of 35–48 Gy in 3–8 fractions. The range of annual LC inspections and overall survival varied, ranging from 71% to 87% and 60% to 78%, respectively.⁹

4.2. SBRT IN EARLY LARYNGEAL CANCER

In early-stage glottic cancer, treatment includes CO₂ laser resection, hemilaryngectomy, and definitive radiotherapy. Laser excision is used in Tis or T1 according to TNM classification to obtain good vocal results, but the involvement of the anterior commissure and larger lesions can be difficult to remove and may be associated with a greater risk of local recurrence and/or the development of voice dysfunction. Radiotherapy is the preferred non-surgical treatment because it provides consistent disease control with potentially better voice function results.¹⁴

The glottis is a possible site for SBRT and selective sparing of the vocal folds unoccupied by cancer and/

or arytenoid cartilage folds. The analysis confirms that the maximum movement of the vocal cords at rest is less than 1.3 mm.¹⁵ Research indicates that treatment may improve local control rates, especially in primary T2 high-risk tumor according to TNM classification.

In early laryngeal cancer, methods have been researched not only to preserve the larynx as an organ, but also to maintain its function and voice quality.⁹ Such target was similar for the researchers from the University of Texas. They were analysing 22 patients with glottis tumor in the stage from Tis to T2, who underwent radiotherapy in 1 of 3 regimens: 50 Gy in 15 fractions, 45 Gy in 10 fractions or 42.5 Gy in 5 fractions. Patient in every regiment undergo treatment using the robotic accelerator (Cyberknife). Treatment was carried out every other day, 3 fractions per week, patients were premedicated with 4 mg of dexamethasone 1 h before radiotherapy, starting with the 2nd fraction. In statistical analysis, LC was comparable for 15 fractions vs 5 fractions, for the median follow-up time of 13 months. Treatment toxicity occurred in 2 cases of patients and it was: hoarseness and dysphagia above grade 2 and it concerned 1 patient in the group with the 10 fraction scheme and 1 in the group with the 5 fraction scheme. It is important to underline the fact that both patients were active smokers.¹⁷ The authors emphasize that single cases of severe toxicity occur primarily in heavy smokers.¹⁸ After 1 year of follow-up, the estimated local control was 82% and overall survival was 100%. Four patients had relapses within the treated glottis, 2 patients with stage cT1 disease had local failure and emergency laser resection was performed in these cases. Two consecutive patients with primary cT2 with spreading subglottal infiltration had a large area of failure and required emergency laryngectomy.¹⁷

Overall, this study shows that stereotactic radiotherapy in early glottal carcinomas may be a short and effective treatment in this diagnosis. The published data suggest that for good local control after radiotherapy, total treatment time is major factor, which in the case of SBRT is limited to less than 2 weeks.¹⁹

During the radiotherapy planning, the radiotherapist contour the area of the tumor which is called gross tumor volume (GTV). Schawartz et al. recommended adding 2 mm of margin to clinical target volume (CTV). However the CTV area is not always covering whole vocal cord and for such reason the authors recommend that in the stage cT2 to contour a whole vocal cord on the same side of the tumor and the paraglottic space. In the case of bilateral vocal cord involvement, the CTV involved the bilateral vocal cords, the anterior

or commissure, and the paraglottic spaces. Arytenoid cartilages were included in the CTV in all lesions within their radius of 2 mm margin, or involving the arytenoid cartilage on the same side. The anterior commissure and 2 mm margin of the contiguous vocal cord on the opposite side were included in the CTV in all lesions within 2 mm of/or involving the vocal cords. The planned target volume (PTV) was defined as CTV plus 3 mm margin. Critical organs by Schwartz et al.¹⁷ identified as: bilateral carotid arteries, arytenoid cartilages, skin, thyroid, and spinal cord.¹⁷

4.3. SBRT AS ADJUVANT TREATMENT AFTER SURGERY

There are no studies on the possibility of using SBRT as postoperative adjuvant treatment, so there is only the possibility of interpolating indications from other locations that suggest that the SBRT site in HNC may take place in the presence of a residual tumor, narrow and/or positive margins.

These questions are to be answered by the STEREO POSTOP study, a non-randomized phase II study within GORTEC association, which began in 2018 and is to last until 2024, on a group of 90 patients. Patients with early-stage of oral and pharyngeal cancer and oral cancer after operation with a high risk of positive margins indicating the need for adjuvant postoperative radiotherapy will be eligible for the study. A total dose of 36Gy was scheduled to be administered from SBRT in 6 fractions. The primary endpoint will be the evaluation of late side effects. Secondary endpoints will include acute toxicity (up to 3 months), local and loco-regional control, disease-free survival and overall survival, patient quality of life, nutritional effect, and predictors of toxicity.²⁰

4.4. SBRT AS A BOOST

The first report on the use of SBRT as a boost after radiotherapy (dose escalation method) was published by Stanford University in 1997 and concerned 11 patients with nasopharyngeal cancer, where 100% local cure was achieved within 21 months. Thereafter, recurrences and/or dissemination of the disease were reported in 35% of patients. In the following years, an update of the report was issued (2003 and 2008), taking into account late complications such as: radiation retinopathy, which was present in 3 patients, carotid aneurysm in 1 patient or temporal lobe necrosis, which occurred in 10 patients, of which 9 patients were advanced T4 disease according to the TNM classification.⁹

A similar area of interest was presented by Dong Soo Lee et. al.,²¹ where in 26 patients with advanced disease and medically inoperable or large residual

tumors in close proximity to critical structures, after completion of primary conventional radiotherapy (median 50.4 Gy, range 39.6–70.2 Gy) used dose escalation with SBRT. During radiotherapy, the median for the prescribed isodose was 80%, and the median dose was 21 Gy (range 10–25 Gy) in 2–5 fractions (median 5), and the post-treatment follow-up was 27.6–80.2 months with a median of 56 months. It is also worth mentioning that the location of the treated areas, which were most often near the base of the skull and in the upper floor of the pharynx, much less often in the area of the oropharynx: the distribution of locations was as follows – nasopharynx, including the skull base for 10 people (38.5%), nasal and/or paranasal cavities, sinuses 8 patients (30.8%), periorbital area 4 patients (15.4%), tongue 3 patients (11.5%), and the oral cavity and pharynx in 1 person (3.8%).²⁰ The authors obtained a response rate of 100%, and in 21 patients (80.8%) it was a complete remission of the disease. Unfortunately, complications were also observed, and so at grade 3 or more, late toxicity occurred in 9 (34.6%) patients. An important factor predicting severe complications was the volume of SBRT areas. The complication rate was also influenced by the combined chemotherapy with conventional radiotherapy in these patients; after SBRT, the total rate of severe late complications was 77.8%. There was a high frequency of serious acute complications – 27%, which is related to the fact that SBRT was used already 2 weeks after radiotherapy – such aggressive treatment in a short time led to unacceptable toxicity. In the conclusions, the authors emphasize that modern SBRT can be used as a RTH boost, but with a certain time interval from the end of primary radiotherapy.²¹

Summing up, the authors gave doses in the range 7-35Gy in 1–5 fractions as a boost after conventional radiotherapy. Such procedure may lead to an increase in the equivalent dose in 2 Gy fractions (EQD2) dose to 90 Gy. Moreover, the biological effective dose (BED) of more than 100 Gy, which influenced improvement in LC. Optimal patient selection is necessary to avoid severe late complications. Furthermore, the patient should have a good response to primary radiotherapy so that the SBRT boost is on the smallest residual lesion, which enables better local control and lower toxicity of the therapy.⁹

4.5. STEREOTACTIC RADIOTHERAPY IN RECURRENT CANCERS OF HNR / REPEAT RADIOTHERAPY WITH SBRT

The treatment of recurrent primary or secondary is challenging, especially in patients previously exposed to radiation. Therefore, there is a growing interest in

the utilization of SBRT. It is important to emphasize that the studies presented herein pertain to patients with specific anatomical locations (skull base, periorbital region, or nasopharynx), where such a technique can be feasibly applied.²¹ However, the high risk of disease recurrence and failure means that work is underway to safely implement high fractional doses to this treatment.

Kawaguci et al.¹² enrolled 22 patients treated with lymph node recurrence and/or metastases and 14 patients with local recurrence without lymph node metastases (N0) for SBRT treatment. The SBRT doses ranged 20–42 Gy in 2–5 fractions. Moreover, the patients received systemic treatment (classical chemotherapy) adjuvant for 1 year. The authors obtained the following results: in case of 9 people (64.3%) complete response was achieved, 1 patient (7.1%) had a partial response to treatment, 1 person had disease stabilization (7.1%) and 3 patients (21.4%) had further disease progression. Among a group of 22 patients with advanced and/or recurrent disease, 10 (45.5%) achieved a complete response with a median follow-up of 2 years. The overall two-year survival rate for patients with lymph node metastases was 12.5%, while it was 78.6% for individuals without metastases.¹²

In a study by Roh et al.²² 36 patients with recurrent tumors of the HNR were treated after primary radiotherapy (median dose 70.2 Gy) using cyberknife in 3 x 10 Gy or 3 x 13 Gy regimens, then fractionation was changed to 5 fractions of 5 Gy or 8 Gy. Complete response was achieved in case of 15 patients (42.9%) and partial response to treatment in 13 (37.1%) patients with median LC and overall survival rates at 1 year of 61.0% and 52.1%, respectively. Among the late side effects, complications of grade 4 in 2 and grade 5 in 1 were observed: osteonecrosis of the mandibular 5 months after SBRT; and twice mucosal necrosis. The authors suggest that the SBRT doses are too high, because 30–39 Gy in 3 fractions corresponds to 80–130 Gy in conventional 2 Gy fractionated radiotherapy, for the α/β ratio 3 Gy and after adjusting the total dose and fractionation protocol to 25–40 Gy in 5 fractions (BED of 40–90 Gy), no late complications were found.²²

Ozyigit et al.²³ analyzed re-radiotherapy in case of 24 patients with SBRT compared to 27 patients qualified for conventional re-radiation therapy. The total dose of 30 Gy was administered in 5 fractions in the stereotactic arm and the median dose in the 3D-CRT group was 57 Gy. The obtained 2-year LCI rates were similar for both arms: SBRT 82% vs 80% for 3D-CRT. The difference the authors found in the reported late side effects was intriguing, which was 21% for SBRT

and 48% for conventional radiotherapy. In conclusion, the authors emphasize that SBRT seems to be an attractive treatment method with a lower degree of late side effects and shorter re-irradiation times.²³

Kress et al.²⁴ described the results in case of 85 patients treated with SBRT with a median dose of 30 Gy (range: 16–41 Gy) in 3 to 5 fractions. A complete response was 36%, a partial response was achieved in a further 33% of patients, and the median interval to prior radiotherapy was 32 months. The overall survival was 51.1% after 1 year and 24% after 2 years. Acute grade 3 toxicity was 2.4% and grade at least 3 late toxicity had an incidence of 5.9%. Moreover, the authors observed that for the time interval from the previous time, irradiation to SBRT lasting greater than or equal to at least 2 years influenced overall survival and was associated with its improvement.²⁴

Comet et al.²⁵ in his study, from June 2007 to January 2010, treated a total of 40 patients for 43 lesions, of which 25 (62.5%) were male. All recurrences or new lesions were considered inoperable and occurred in the previously irradiated area (<65 mm) with a median dose of 66 Gy. In addition, 70% had previously undergone surgery and 57% had prior chemotherapy during their initial treatment. Median time between initiation and retreatment was 31.6 months (range 7.9–263.4 months). The anatomical sites of recurrence were: oral cavity (20.0%), oropharynx (10.0%), lower pharynx (7.5%), base of skull (17.5%), nasopharynx (20.0%), sinuses (5.0%), larynx (5.0%) and other sites (15.0%). Importantly, the median size of the lesion was 29.5 mm (range 8.0–85.0 mm), and the median volume of PTV was 64.1 cm³ (range 4.7–295.6 cm³). The median duration of treatment was 12 days (range 11–98 days). The median follow-up was 25.6 months and it concerned 34 patients in whom tumor response to treatment could be assessed. The median overall survival was 13.6 months and the response rate was 79.4% (15 CR and 12 PR).²⁵

The range of doses used in individual studies in the case of SBRT as repeated radiotherapy differs between authors and ranges from 13–24 Gy in 1 fraction most often, and in several fraction patterns from 19.5 Gy to 50 Gy in 3 to 8 fractions.²⁶

The authors of the studies emphasize that repeated radiotherapy with stereotactic radiotherapy is quite well tolerated, but late complications in critical organs develop relatively shortly after SBRT, and their intensity is not observed in primary operated patients.¹² The following complications include: mucositis, tissue necrosis, bone necrosis, fistulas, the occurrence of NVG-glaucoma (it progresses approximately 2–3

years after SBRT) and one of the most serious adverse events – carotid artery rupture. In conclusion, the authors emphasize that high α/β in most tumors of this localization and low α/β in the surrounding organs and tissues, as well as hypofractionation with extremely high fractional doses, may be inappropriate patterns for this localization and their selection should be approached with great care.^{12,21,26} Hence, new guidelines have been established for the deposition of maximum doses, mean doses, and specific volume constraints within critical organs during hypofractionation, for example. UK Consensus on Normal Tissue Dose Constraints for Stereotactic Radiotherapy, G.G or Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) (Tables 2 and 3).^{27,28}

Although there are no randomized, phase 3 controlled trials of SBRT in re-irradiation, there are phase 2 studies and large observational studies that indicate that SBRT may be a treatment option for re-irradiation in HNC.²

A working group established by the American Association of Medical Physicists to investigate the likelihood of tumor control for SBRT in head and neck tumors conducted a systematic review of the available literature.

SBRT has emerged as a viable strategy for local re-irradiation of recurrent previously irradiated HNC. Data from over 300 cases in 8 publications suggest that there is a relationship between dose and better

LC and the likelihood of improvement in overall survival, and a dose range of 35–45 Gy (in 5 fractions) is recommended compared to total doses below 30 Gy.²⁹

4.6. CAROTID ARTERY RUPTURE – A SERIOUS COMPLICATION OF REPEATED RADIOTHERAPY

Repeated radiotherapy, whether conventional or SBRT, may lead to serious adverse events, such as carotid artery rupture, which should always be considered when qualifying patients for treatment.³⁰ Carotid artery rupture (CBOS) is a fatal complication and is a problem with irradiation, especially with SBRT.¹ It is estimated that the occurrence of such incident reaches even 10% to 20% of repeated radiotherapy.²⁹

Yamazaki et al.³¹ indicate factors influencing the growth of rupture of the cervical vessels and include: repeated radiotherapy in the area of the lymph nodes, a tumor involving minimum half of the circumference of the carotid artery, ulceration in the area qualified for repeated radiotherapy.³¹

Other factors that may influence the occurrence of carotid artery rupture are: infection, pharyngocutaneous fistula formation, tumor progression, diffuse involvement, and/or mucosal ulceration. McDonald et al.³² in his study described 41 such cases out of 1554 treated patients, which amounted to 2.6% of which it should be emphasized that three-fourths were fatal.³²

Table 2. Normal tissue constraints for SBRT.²⁷

Organ at risk	Volume	1 fraction (Gy)	3 fractions (Gy)	5 fractions (Gy)	8 fractions (Gy)
Spinal cord	D _{max} (Gy)	14	22.5	28	
	D0.35cc (Gy)	10	15.9	22	30
	D1.2cc (Gy)	8	13	15.6	
Optic pathway	D _{max} CC	<10 <0.2 cm ³ >8	<17.4 <0.2 cm ³ >15.3	<25 <0.2 cm ³ >23	
	D _{max} CC	<12 <0.5 cm ³ >10	<23.1 <0.5 cm ³ > 18	<31 <0.5 cm ³ > 23	
Brainstem	D _{mean}		<6		
	D _{max}	<8			
Lens	D _{max}	<2	<3	<3	
Inner ear	D _{max}	<9	<17.1	<25	
Parotid gland					
Esophagus	D _{max} (Gy)	15.4	25.2	35	40
	D5cc (Gy)	11.9	17.7	19.5	

Table 3. QUANTEC Stereotactic radiosurgery (single fraction).²⁸

Critical structure	Volume	Dose/Volume	Max dose	Toxicity rate	Toxicity endpoint
Brain		V12 <5-10 cc		<20%	Symptomatic necrosis
Brain stem (acoustic tumors)			<12.5 Gy	<5%	Neuropathy or necrosis
Optic Nerve/chaism			<12 Gy	<10%	Optic neuropathy
Spinal cord (single-fx)			13 Gy	1%	Myelopathy
Spinal cord (hypo-fx)			20 Gy	1%	Myelopathy
Cochlea	Prescription dose	≤14 Gy		<25%	Sensory-neural hearing loss

It seems that the maximum dose for the carotid artery below 33 Gy may reduce the risk of CBOS, special care should be taken in the case of tumors in the vicinity of the circumference of the carotid artery with over 180° carotid circumference receiving at least 30 Gy.^{2,33}

4.7. 'IDEAL PATIENT' PROFILE FOR SBRT APPLICATION

Ward et al.³⁴ published normograms in which the authors assessed the risk of developing late side effects and selecting patients for re-radiotherapy. The extent and intensity of late toxicity are influenced by factors such as: the dose of radiotherapy during the first course, organ dysfunction, previous surgery, tumor localisation, age, recurrence or a second primary neoplasm. Based on normograms, the authors estimated that the risk of disease progression or death is four fold higher than the occurrence of late toxicity.³⁴

In addition, the authors divided patients with cancers of the head and neck region into three classes:

- (1) Class I patients with a period of time longer than 2 years from the first treatment, i.e. tumor resection (2 years OS 61.9% with 95%CI: 51, 9–73.9%);
- (2) Class II are patients with an elapsed time of more than 2 years from the first treatment but treatment considered an unresectable tumor or patients with a duration of less than 2 years but with an intact organ (2 years OS 40.0% with 95%CI: 33.9–47.2%);
- (3) Class III includes patients with less than 2 years from the first treatment with organ dysfunction (2-year OS 16.8%; 95%CI: 10.0–28.1%).³⁴

Based on the analysis of the literature the authors have formulated the following conclusion regarding patients eligible for SBRT:

- (1) Treatment should be considered for patients receiving treatment more than 2 years after their primary treatment.
- (2) In cases with a shorter time interval, a minimum of 6 months should elapse before considering SBRT.
- (3) If feasible, tumor resection should be pursued.
- (4) In cases of non-resectable tumors, preservation of the functional organ should be a priority

4.8. PLANNING OF SBRT RADIATION THERAPY

Planning of radiotherapy must be carried out with the utmost care using immobilization dedicated to stereotactic treatment and this localization (standard 5-point mask), with 4-D computed tomography to plan treatment with motion correction and using all possible diagnostic imaging tests (CT fusion to planning with: CT, MRI, PET/CT, PET/MR). It is recommended to contour only the GTV disc area in the SBRT technique:

no CTV, no elective area of the lymph nodes. Margins between GTV and PTV of 1.5–2.0 mm may be sufficient for tumors located in the region of the base of skull. Margins between GTV and PTV of 2.0–2.5 mm are added for locations within the neck and/or mucosa. To minimize tissue damage, the dose is prescribed for an isodose of 90%–95%. The currently recommended total dose for SBRT of the HNR is 35–40 Gy in 5 fractions twice a week.^{2,26} Daily CBCT and kV testing is recommended before treatment and in the middle of treatment to reduce inter-fraction variability.

4.9. FAILURE AFTER SBRT

There are few reports on the treatment regimens in the event of failure of stereotactic radiotherapy, each case should be approached individually, and the choice of therapy should be selected with the participation of interdisciplinary oncology council.

5. CONCLUSIONS

SBRT is relatively safe and effective, especially in those cancers where the survival time with the cancer is relatively long, moreover, the location of the critical organs around the target of the therapy and the dose deposited in the critical organs is important. Summarizing, the clinical situations in which treatment with stereotactic SBRT radiotherapy in HNC should be considered are: presence of a residual tumor, narrow and/or positive margins, local and/or regional recurrence, boost after RTH with poor tumor response, early carcinoma of the glottis to preserve the voice function, disqualification from the surgery, disqualification and/or refusal to consent to conventional radiotherapy. The indications for stereotactic radiotherapy of HNC based on patient-related factors include: old age, comorbidities, logistical difficulties in traveling for treatment, poor family support and/or low economical status, lack of consent to other forms of therapy, lack of consent for a long time treatment.⁹

CONFLICT OF INTEREST

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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